Application No.: 10/520,457

Filing Date: November 30, 2005

AMENDMENTS TO THE CLAIMS

 (Currently amended) A method for the preparation of virus-inactivated thrombin comprising the steps of:

- (a) subjecting a solution comprising prothrombin and faetor <u>Factor X</u> to a virus inactivation procedure, by adding solvent and detergent to said solution, wherein the solvent is tri-n-butyl phosphate (TNBP);
- (b) loading the product of step (a) onto an anion exchange medium_wherein the prothrombin and Factor X bind to the anion exchange medium;
- (c) washing the anion exchange medium to remove <u>TNBP and detergent</u> reagents used for the virus inactivation-procedure in step (a), and
- (d) activating the <u>Factor X prothrombin</u> on the anion exchange medium to form <u>Factor Xa thrombin</u> by addition of metal ions, <u>wherein the Factor Xa then activates the</u> <u>prothrombin to yield thrombinwherein thrombin with a specific activity of at least 2000</u> <u>International Units per mg of protein is generated</u>.
- (Previously presented) The method according to claim 1, wherein the solution comprising prothrombin and factor X is a prothrombin complex.
- (Currently amended) A method for the preparation of virus-inactivated thrombin comprising the steps of:
 - (a) subjecting a solution comprising factor X to a virus inactivation procedure, by adding solvent and detergent to said solution, wherein the solvent is <u>TNBPtri-n-butyl</u> phosphate;
 - (b) loading the product of step (a) onto an anion exchange medium wherein the Factor X binds to the anion exchange medium;
 - (c) washing the anion exchange medium to remove <u>TNBP and detergent</u> reagents used for the virus inactivation procedure in step (a);
 - (d) activating the factor X on the anion exchange medium to form factor Xa by addition of metal ions; and
 - (e) loading virus-inactivated prothrombin onto the anion exchange medium such that the activated Factor Xa converts prothrombin to thrombin, wherein thrombin with a specific activity of at-least-2000 International Units per mg of protein is generated.

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(Previously presented) The method according to claim 1 or 3 wherein the metal ions
are divalent metal ions

- (Previously presented) The method according to claim 4 wherein the divalent metal ions are magnesium and/or calcium ions.
- (Previously presented) The method according to claim 1, further comprising the step of
 - (e) selectively eluting the thrombin from the anion exchange medium.
- (Previously presented) The method according to claim 6, further comprising the steps of
 - (f) passing the product of step (e) through a filter which retains pathogens;
 - (g) adding a divalent metal ion and a carbohydrate to the product of step (f), and
 - (h) freeze-drying and heat-treating the product of step (g) to inactivate viruses.
 - 8-13. (Canceled)
- 14. (Previously presented) The method according to claim 3, further comprising the step of
 - (f) selectively eluting the thrombin from the anion exchange medium.
- 15. (Previously presented) The method according to claim 14, further comprising the steps of
 - (g) passing the product of step (f) through a filter which retains pathogens;
 - (h) adding a divalent metal ion and a carbohydrate to the product of step (g), and
 - (i) freeze-drying and heat-treating the product of step (h) to inactivate viruses.
- 16. (Currently amended) A method for the preparation of virus-inactivated thrombin comprising the steps of:
 - (a) loading a solution comprising prothrombin and factor X onto an anion exchange medium; and
 - (b) subjecting the prothrombin and factor X to a virus inactivation procedure by adding solvent and detergent to said prothrombin and factor X on the anion exchange medium, wherein the solvent is TNBPtri-n-butyl-phosphate;
 - (c) washing the anion exchange medium to remove the TNBP and detergent reagents used for the virus inactivation procedure in step (b), and

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(d) activating the Factor X on the anion exchange medium to form Factor Xa by addition of metal ions, wherein the Factor Xa then activates the prothrombin to yield thrombin, wherein thrombin with a specific activity of at least 2000 International Units per mg of protein is generated.

- 17. (Previously presented) The method according to claim 16 wherein the metal ions are divalent metal ions
- 18. (Previously presented) The method according to claim 17 wherein the divalent metal ions are magnesium and/or calcium ions.
- 19. (Previously presented) The method according to claim 16, further comprising the step of
 - (e) selectively eluting the thrombin from the anion exchange medium.
- 20. (Previously presented) The method according to claim 19, further comprising the steps of
 - (f) passing the product of step (e) through a filter which retains pathogens;
 - (g) adding a divalent metal ion and a carbohydrate to the product of step (f), and
 - (h) freeze-drying and heat-treating the product of step (g) to inactivate viruses.
- 21. (Currently amended) A method for the preparation of virus-inactivated thrombin comprising the steps of:
 - (a) loading a solution comprising Factor X onto an anion exchange medium; and
 - (b) subjecting the Factor X to a virus inactivation procedure by adding solvent and detergent to said Factor X on the anion exchange medium, wherein the solvent is TNBPtri-n-butyl-phosphate,
 - (c) washing the anion exchange medium to remove the TNBP and detergent reagents used for the virus inactivation procedure in step (b);
 - (d) activating the Factor X on the anion exchange medium to form factor Xa by addition of metal ions; and
 - (e) loading virus-inactivated prothrombin onto the anion exchange medium such that the activated Factor Xa converts prothrombin to thrombin, wherein thrombin with a specific activity of at least 2000 International Units per mg of protein is generated.

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22. (Previously presented) The method according to claim 21 wherein the metal ions are divalent metal ions.

- 23. (Previously presented) The method according to claim 22 wherein the divalent metal ions are magnesium and/or calcium ions.
- 24. (Previously presented) The method according to claim 21, further comprising the step of
 - (e) selectively eluting the thrombin from the anion exchange medium.
- 25. (Previously presented) The method according to claim 24, further comprising the steps of
 - (f) passing the product of step (e) through a filter which retains pathogens;
 - (g) adding a divalent metal ion and a carbohydrate to the product of step (f), and
 - (h) freeze-drying and heat-treating the product of step (g) to inactivate viruses.
- 26. (Previously presented) The method according to Claim 1, wherein step (d) is performed without addition of phospholipids.
- 27. (Previously presented) The method according to Claim 3, wherein step (d) is performed without addition of phospholipids.
- 28. (Previously presented) The method according to Claim 16, wherein step (d) is performed without addition of phospholipids.
- 29. (Previously presented) The method according to Claim 21, wherein step (d) is performed without addition of phospholipids.